

**WHAT IS CLAIMED IS:**

1. A method of increasing sensitivity of stem cells to a chemoattractant, the method comprising exposing the stem cells to a matrix metalloprotease or an active portion thereof, which is capable of increasing a level of at least one chemoattractant receptor of the stem cells to thereby increase the sensitivity of the stem cells to the chemoattractant.
2. The method of claim 1, wherein said at least one chemoattractant receptor is CXCR4.
3. The method of claim 1, wherein said matrix metalloprotease is selected from the group consisting of MMP-2, MMP-3, MMP-9, MMP-10, MMP-13 and MMP-14.
4. The method of claim 1, wherein said matrix metalloprotease is selected from the group consisting of MMP-2 and MMP-9.
5. The method of claim 1, wherein the stem cells are hematopoietic stem cells.
6. The method of claim 5, wherein said hematopoietic stem cells are CD34<sup>+</sup> hematopoietic stem cells.
7. The method of claim 6, wherein said hematopoietic stem cells are CD34<sup>+</sup>/CD38<sup>low</sup> hematopoietic stem cells.
8. The method of claim 1, wherein the stem cells are mesenchymal stem cells.
9. The method of claim 1, wherein said exposing the stem cells to said matrix metalloprotease or said active portion thereof, is effected by:

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- (i) expressing a polynucleotide encoding said matrix metalloprotease or an active portion thereof in the stem cells; and/or
- (ii) contacting the stem cells with said matrix metalloprotease or an active portion thereof.

10. A method of treating a disorder requiring cell or tissue replacement, the method comprising providing to a subject in need thereof a therapeutically effective amount of stem cells treated with a matrix metalloprotease or an active portion thereof, which is capable of increasing a level of at least one chemoattractant receptor of the stem cells, thereby treating the disorder requiring cell or tissue replacement in the subject.

11. The method of claim 10, wherein said at least one chemoattractant receptor is CXCR4.

12. The method of claim 10, wherein said matrix metalloprotease is selected from the group consisting of MMP-2, MMP-3, MMP-9, MMP-10, MMP-13 and MMP-14.

13. The method of claim 10, wherein said matrix metalloprotease is selected from the group consisting of MMP-2 and MMP-9.

14. The method of claim 10, wherein the stem cells are hematopoietic stem cells.

15. The method of claim 14, wherein said hematopoietic stem cells are CD34<sup>+</sup> hematopoietic stem cells.

16. The method of claim 15, wherein said hematopoietic stem cells are CD34<sup>+</sup>/CD38<sup>-/low</sup> hematopoietic stem cells.

17. The method of claim 10, wherein said stem cells are mesenchymal stem cells.

18. A culture medium suitable for increasing the sensitivity of stem cells to a chemoattractant, the culture medium comprising a matrix metalloprotease or an active portion thereof which is capable of increasing a level of at least one chemoattractant receptor of the stem cells and a buffer solution suitable for stem cell culturing.

19. The culture medium of claim 18, further comprising a differentiation inhibiting factor.

20. The culture medium of claim 18, further comprising serum or serum replacement.

21. The culture medium of claim 18, further comprising an agent selected from the group consisting of SCF, HGF and IL-6.

22. Use of a matrix metalloprotease or an active portion thereof for the manufacture of a medicament for increasing homing of stem cells to a target tissue.

23. The use of claim 22, wherein said stem cells are hematopoietic stem cells.

24. The use of claim 23, wherein said hematopoietic stem cells are CD34<sup>+</sup> hematopoietic stem cells.

25. The use of claim 24, wherein said hematopoietic stem cells are CD34<sup>+</sup>/CD38<sup>-/low</sup> hematopoietic stem cells.

26. The use of claim 22, wherein said stem cells are mesenchymal stem cells.

27. The use of claim 22, wherein said target tissue is selected from the group consisting of bone marrow, blood vessel, heart, lung, liver, pancreas, kidney, nervous system, skin, bone and skeletal muscle.

28. The use of claim 22, wherein said matrix metalloprotease is selected from the group consisting of MMP-2, MMP-3, MMP-9, MMP-10, MMP-13 and MMP-14.

29. The method of claim 22, wherein said matrix metalloprotease is selected from the group consisting of MMP-2 and MMP-9.

30. A method of generating stem cells suitable for transplantation, the method comprising:

- (a) collecting stem cells;
- (b) exposing said stem cells to a matrix metalloprotease or an active portion thereof; and
- (c) isolating stem cells having CXCR4 levels above a predetermined threshold, to thereby generate stem cells suitable for transplantation.

31. The method of claim 30, wherein collecting said stem cells is effected by:

- (i) a stem cell mobilization procedure; and/or
- (ii) a surgical procedure.

32. The method of claim 30, wherein said matrix metalloprotease is selected from the group consisting of MMP-2, MMP-3, MMP-9, MMP-10, MMP-13 and MMP-14.

33. The method of claim 30, wherein said matrix metalloprotease is selected from the group consisting of MMP-2 and MMP-9.

34. The method of claim 30, wherein said stem cells are hematopoietic stem cells.

35. The method of claim 34, wherein said hematopoietic stem cells are CD34<sup>+</sup> hematopoietic stem cells.

36. The method of claim 34, wherein said hematopoietic stem cells are CD34<sup>+</sup>/CD38<sup>-low</sup> hematopoietic stem cells.

37. The method of claim 30, wherein said stem cells are mesenchymal stem cells.

38. The method of claim 30, wherein said exposing said stem cells to said matrix metalloprotease or said active portion thereof, is effected by:

- (i) expressing a polynucleotide encoding said matrix metalloprotease or said active portion thereof in said stem cells; and/or
- (ii) contacting said stem cells with said matrix metalloprotease or said active portion thereof.

39. The method of claim 30, wherein said isolating stem cells having CXCR4 levels above said predetermined threshold is effected by FACS.

40. The method of claim 31, further comprising determining homing capabilities of said stem cells having CXCR4 levels above said predetermined threshold following step (c).

41. A nucleic acid construct comprising a first polynucleotide sequence encoding a matrix metalloprotease or an active portion thereof and an inducible cis-acting regulatory element for directing expression of said polynucleotide in cells.

42. The nucleic acid construct of claim 41, wherein said inducible cis-acting regulatory element is a shear stress activation element.

43. The nucleic acid construct of claim 41, further comprising a second polynucleotide sequence being translationally fused to said first polynucleotide

sequence, said second polynucleotide sequence encoding a signal peptide capable of directing secretion of said matrix metalloprotease or said active portion thereof out of said cells.

44. The nucleic acid construct of claim 41, wherein said matrix metalloprotease is selected from the group consisting of MMP-2, MMP-3, MMP-9, MMP-10, MMP-13 and MMP-14.

45. The nucleic acid construct of claim 41, wherein said matrix metalloprotease is selected from the group consisting of MMP-2 and MMP-9.

46. A eukaryotic cell comprising the nucleic acid construct of claim 41.

47. A cell-line comprising stem cells transformed to express an exogenous polynucleotide encoding a matrix metalloprotease.

48. The cell-line of claim 47, wherein said matrix metalloprotease is selected from the group consisting of MMP-2, MMP-3, MMP-9, MMP-10, MMP-13 and MMP-14.

49. The cell-line of claim 47, wherein said matrix metalloprotease is selected from the group consisting of MMP-2 and MMP-9.

50. The cell-line of claim 47, wherein said stem cells are hematopoietic stem cells.

51. The cell-line of claim 50, wherein said hematopoietic stem cells are CD34<sup>+</sup> hematopoietic stem cells.

52. The cell-line of claim 51, wherein said hematopoietic stem cells are CD34<sup>+</sup>/CD38<sup>low</sup> hematopoietic stem cells.

53. The cell-line of claim 47, wherein said stem cells are mesenchymal stem cells.
54. A method of increasing sensitivity of stem cells to a chemoattractant, the method comprising, upregulating an expression or activity of at least one endogenous MMP of the stem cells to thereby increase the sensitivity of the stem cells to the chemoattractant.
55. A method of increasing sensitivity of stem cells to a chemoattractant in a subject in need, the method comprising, administrating said patient with at least one matrix metalloprotease or an active portion thereof.
56. The method according to claim 55, wherein said matrix metalloprotease is selected from the group consisting of MMP-2, MMP-3, MMP-9, MMP-10, MMP-13 and MMP-14.
57. The method according to claim 56, wherein said matrix metalloprotease is selected from a group consisting of MMP-2, and MMP-9.
58. A method of generating stem cells suitable for transplantation, the method comprising:
  - (a) collecting stem cells; and
  - (b) exposing said stem cells to MMP or an active portion thereof.
59. A pharmaceutical composition comprising at least one matrix metalloprotease or an active portion thereof for treating a disorder requiring cell or tissue replacement.
60. A pharmaceutical composition according to claim 59, wherein wherein said matrix metalloprotease is selected from a group consisting of MMP-2, and MMP-9.
61. A pharmaceutical composition according to claim 60, wherein wherein said matrix is MMP-2.
62. A pharmaceutical composition according to claim 60, wherein wherein said matrix is MMP-9.